

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4	10/656530 and subject	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 17:07
L2	2	10/656530 and (structural adj similarity)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 17:07
S379	2	"6028189".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/10/12 23:29
S380	4	10/656530	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 11:28
S381	0	10/656530 and (strucutral adj similarity)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 11:33
S382	2	10/656530 and (structural adj similarity)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 11:48
S383	4	10/656530 and (properl\$)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 11:55
S386	4	10/656530 and (level near decreas\$)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 15:12

## EAST Search History

S387	3	10/656530 and (Ghrelin)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 15:22
S388	4	10/656530 and (antagonist)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 15:44
S389	0	(growth adj hormone adj secretagogue adj receptor) near (antagonist or agonist or analog or compound) same igf	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 15:51
S390	81	(growth adj hormone adj secretagogue adj receptor) near (antagonist or agonist or analog or compound)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 16:19
S391	111	(ghrelin adj receptor) near (antagonist or agonist or analog or compound)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 16:37
S392	157	mk-0677 same (growth adj hormone)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 17:01
S393	105	S392 and merck	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 18:44
S394	32	mk-0677 same ((ghrelin or secretagogues) adj receptor)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 17:05

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S39 5	2	"6432920".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/05 18:44
S39 6	2	"5723286".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:00
S39 7	2	(distefano or bayley or cannon).in. and (GH or (growth adj hormone)). clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:17
S39 8	2	(distefano or bayley or cannon).in. and (IGF or (insulin adj like adj growth)).clm.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:17
S39 9	2	"2005187237".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:14
S40 0	2	"20050187237".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:15
S40 1	2	"20050261332".pn.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:15
S40 2	249	(distefano or bayley or cannon).in. and (GH or (growth adj hormone))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 14:17

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S40 3	6	(distefano or bayley or cannon).in. and ((GH or (growth adj hormone)) near (IGF or (insulin adj like adj growth)))	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/18 16:09
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FILE 'CAPLUS' ENTERED AT 14:06:51 ON 18 DEC 2006

	E DISTEFANO P/IN, AU
L1	28 S E4 OR E6 OR E7
	E BAYLEY, C/IN, AU
	E BAYLEY, CYNTHIA/IN, AU
	E BAYLEY C/IN, AU
	E BAYLEY CYNTHIA/IN, AU
L2	4 S E5 OR E6
	E CANNON L/IN, AU
L3	31 S E4 OR E8 OR E9 OR E10
L4	59 L1 OR L2 OR L3
L5	4 L4 AND ((GROWTH (A) HORMONE) OR GH)
L6	4 S L5 AND PATENT/DT



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Search	Most Recent Queries	Time	Result
<a href="#">#14</a> Search growth hormone secretagogue receptor Limits: Review		16:22:01	<a href="#">104</a>
<a href="#">#19</a> Search ghrelin receptor Limits: Review		16:21:06	<a href="#">89</a>
<a href="#">#13</a> Search growth hormone secretagogue receptor Limits: Review		16:01:26	<a href="#">964</a>
<a href="#">#10</a> Related Articles for PubMed (Select 7624358)		15:51:49	<a href="#">107</a>
<a href="#">#9</a> Search growth hormone secretagogue receptor and antagonist		15:24:03	<a href="#">46</a>
<a href="#">#8</a> Search growth hormone secretagogues receptor and antagonist		15:23:31	<a href="#">13</a>
<a href="#">#5</a> Search growth hormone secretagogues and antagonist		15:15:00	<a href="#">20</a>
<a href="#">#1</a> Search Ghrelin receptor antagonist		15:11:39	<a href="#">44</a>

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☐ 1: CNS Neurol Disord Drug Targets. 2006 Jun;5(3):335-43.



Links

**Growth hormone secretagogue (ghrelin-) receptors--a complex drug target for the regulation of body weight.**

**Nogueiras R, Perez-Tilve D, Wortley KE, Tschop M.**

Department of Pharmacology, German Institute of Human Nutrition, Potsdam, Germany.

The growth hormone secretagogue receptor (GHS-R) is expressed in several tissues and seems to mediate the different actions of the synthetic growth hormone secretagogues (GHS) and the endogenous ligand of this receptor, ghrelin. The GHS-R belongs to the family of G-protein coupled receptors (GPCR). Two different receptor variants, type 1a and 1b, have been described and they seem to mediate different actions in different tissues. In addition to their functions on growth hormone (GH) secretion and food intake, ghrelin and its receptor are involved in several cardiovascular mechanisms, pancreatic functions, adipogenesis, gonadal function, immune system actions or tumoral cells. This review will summarize data regarding the structure of the GHS-R gene, reports investigating the expression, control and functions of the GHS-R in various tissues, and studies of the underlying transcriptional mechanisms and the genetic manipulation of both ghrelin and GHS-R. Thus, it seems clear the possibility that ghrelin and/or GHS analogs, acting as either agonists or antagonists on different activities, might have clinical impact.

PMID: 16787234 [PubMed - indexed for MEDLINE]

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A novel growth hormone secretagogue-1a receptor antagonist that blocks ghrelin-induced growth hormone secretion but induces increased body weight gain. 2005]

Ghrelin: more than a natural GH secretagogue and/or an orexigenic factor. [Clin Endocrinol (Oxf). 2005]

Ghrelin and synthetic growth hormone secretagogues are cardioactive molecules with identities and differences. [Semin Vasc Med. 2004]

Expression of ghrelin and its functional receptor, the type 1a growth hormone secretagogue receptor, in normal human testis and testicular tumors. [J Clin Endocrinol Metab. 2004]

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☐ 1: [J Clin Endocrinol Metab. 1996 Aug;81\(8\):2776-82.](#)

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[J Clin Endocrinol Metab. 1996 Aug;81\(8\):2773-5.](#)

**Effects of a 7-day treatment with a novel, orally active, growth hormone (GH) secretagogue, MK-677, on 24-hour GH profiles, insulin-like growth factor I, and adrenocortical function in normal young men.**

**Copinschi G, Van Onderbergen A, L'Hermite-Baleriaux M, Mendel CM, Caufriez A, Leproult R, Bolognese JA, De Smet M, Thorner MO, Van Cauter E.**

Center for the Study of Biological Rhythms, Universite Libre de Bruxelles, Belgium.

To assess the effects of prolonged administration of a novel analog of GH-releasing peptide (MK-677), nine healthy young men participated in a randomized, double blind, three-period cross-over comparison of orally administered placebo and 5- and 25-mg doses of MK-677. Each period involved bedtime administration of the drug for 7 consecutive days. At the end of each period, plasma levels of insulin-like growth factor I (IGF-I) and IGF-binding protein-3 (IGFBP-3) were measured at 0745 h, and 24-h profiles of plasma GH and cortisol were obtained at 15-min intervals together with the 24-h urinary excretion of free cortisol. Profiles of plasma free cortisol were calculated at hourly intervals. The amounts of GH secreted were similar in all three conditions, but GH pulse frequency was increased with both dosages of the drug, primarily because of an increase in the number of low amplitude pulses. Plasma IGF-I levels were increased in a dose-dependent manner, whereas IGFBP-3 levels were increased only with the highest dosage. There was a positive relationship between GH pulse frequency and IGF-I increase. Except for an advance in the nocturnal nadir and in the morning elevation, MK-677 had no effect on cortisol profiles. In particular, 24-h mean levels of plasma total and free cortisol and urinary excretion of free cortisol were similar under all conditions. The present data suggest that the use of MK-677 for the treatment of relative somatotrophic deficiency, particularly in older adults compromised by such deficiency, deserves further investigation.

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Stimulation of the growth hormone (GH)-insulin-like growth factor I axis by daily oral administration of a GH secretagogue (MK-677) in healthy elderly subjects. [J Clin Endocrinol Metab. 1996](#)

MK-0677, a potent, novel, orally active growth hormone (GH) secretagogue: GH, insulin-like growth factor I, and other hormonal responses in beagle dogs. [Endocrinology. 1996](#)

Oral administration of growth hormone (GH) releasing peptide-mimetic MK-677 stimulates the GH/insulin-like growth factor-I axis in selected GH-deficient adults. [J Clin Endocrinol Metab. 1997](#)

MK-677, an orally active growth hormone secretagogue, reverses diet-induced catabolism. [J Clin Endocrinol Metab. 1998](#)

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☐ 1: Curr Opin Drug Discov Devel. 2006 Jul;9(4):509-15.

Links

**Growth hormone secretagogue receptor antagonists as anti-obesity therapies? Still an open question.**

**Zhao H, Liu G.**

Abbott Laboratories, Metabolic Disease Research, Global Pharmaceutical Research and Development, 100 Abbott Park Road, Abbott Park, IL 60064-6098, USA. Hongyu.zhao@abbott.com

Ghrelin was recently de-orphaned as an endogenous ligand of growth hormone secretagogue receptor (GHS-R), and is implicated as a short-term meal initiator and a long-term energy balance regulator. Administration of ghrelin causes increases in food intake and body weight in both rodents and humans. Inhibiting its actions with GHS-R anti-sense oligonucleotides, anti-ghrelin antibodies, and peptide antagonists leads to decreased food intake and weight loss in rodents. Despite the much-publicized promise of providing a novel approach for anti-obesity treatment, limited progress has been made in developing small-molecule GHS-R antagonists and no such compound has been advanced to clinical trials. This review will summarize the recent progress in small-molecule GHS-R antagonists and offer some insight into this area of research based on the experience at Abbott Laboratories.

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Growth hormone secretagogue (ghrelin-) receptors--a complex drug target for the regulation of body weight. CNS Neurol Disord Drug Targets. 2006]

Ghrelin, growth and obesity. [Ann Med. 2002]

A novel growth hormone secretagogue-1a receptor antagonist that blocks ghrelin-induced growth hormone secretion but induces increased body weight gain. J Neuroendocrinology. 2005]

The promise of ghrelin antagonism in obesity treatment. Drug News Perspect. 2006]

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